In-Depth

Overview

Points To Remember About Rheumatoid Arthritis

- Rheumatoid arthritis is a disease that causes pain, swelling, and stiffness in your joints. This disease often occurs in more than one joint and can affect any joint in the body. If you have this disease, you may feel sick and tired, and sometimes get fevers.
- Anyone can get arthritis, but it occurs more often in women and is most common in older people.
- Genes, environmental factors, and hormones may play roles in the development of rheumatoid arthritis.
- Treatment may involve medicine, surgery, and alternative therapies.
- Regular rest, joint care, activity, a healthy diet, and reduced stress can ease symptoms.

Rheumatoid arthritis, sometimes referred to as RA, is an inflammatory disease that causes pain, swelling, stiffness, and loss of function in the joints. It occurs when the immune system, which normally helps protect the body from infection and disease, attacks the membrane lining the joints.

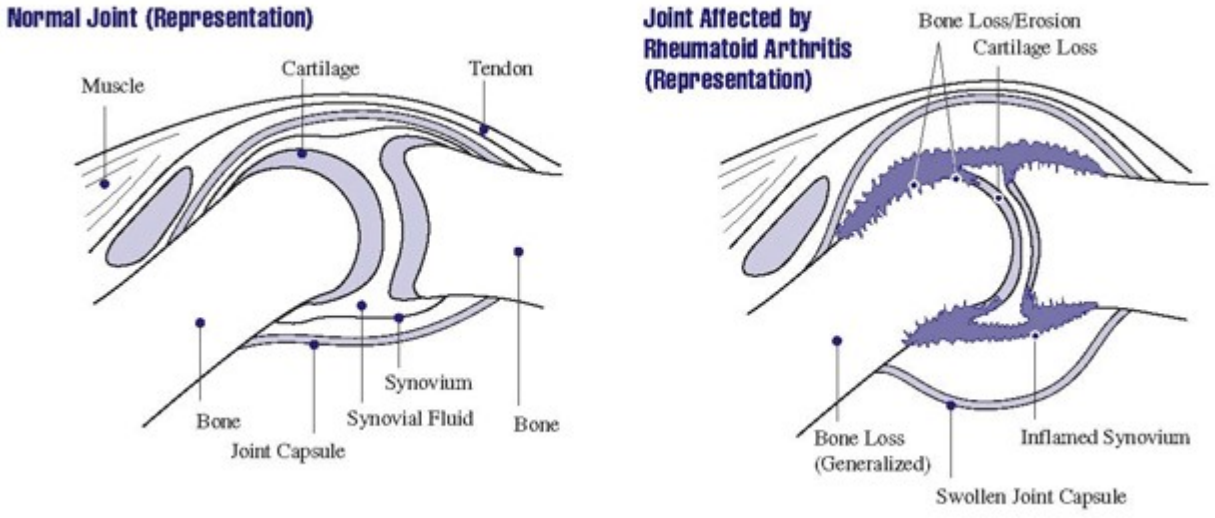
Rheumatoid arthritis is different from other kinds of arthritis in several ways. For example:

- Rheumatoid arthritis generally occurs in a symmetrical pattern, meaning that if one knee or hand is involved, the other one also is.
- Rheumatoid arthritis often affects the wrist joints and the finger joints closest to the hand.
- Rheumatoid arthritis can also affect other parts of the body besides the joints, such as the heart, lungs, blood, nerves, eyes, and skin.
- People with rheumatoid arthritis may have fatigue, occasional fevers, and a loss of appetite.

Fortunately, current treatments allow most people with the disease to lead active and productive

lives. In recent years, research has led to a new understanding of rheumatoid arthritis, which may result in even better ways to treat the disease.

What happens in rheumatoid arthritis?



Rheumatoid arthritis is an autoimmune disease (auto means self). The immune system attacks joint tissues for unknown reasons. Rheumatoid arthritis occurs when:

- White blood cells in the immune system travel to tissue that surrounds the joint, called synovium, and cause inflammation.
- The normally thin synovium becomes thick, making the joint swollen, red, painful, and sometimes warm to the touch.
- As rheumatoid arthritis progresses, the inflamed synovium invades and destroys the cartilage and bone within the joint.
- The surrounding muscles, ligaments, and tendons that support and stabilize the joint become weak and don’t work normally. This leads to pain and joint damage.

Researchers now believe that rheumatoid arthritis begins to damage the bones within the joint during the first year or two that a person has the disease. This is one reason why early diagnosis and treatment are so important.

Who Gets

About 1.5 million people, or about 0.6 percent of the U.S. adult population, have rheumatoid arthritis. Rheumatoid arthritis is more common among certain groups:

- **Age:** The disease often begins in middle age and is more common in older adults. However, older teenagers and young adults may also get the disease. Children and younger teenagers may be diagnosed with juvenile idiopathic arthritis, a condition related to rheumatoid arthritis.
- **Sex:** Like some other forms of arthritis, rheumatoid arthritis is more common among

women than men. About two to three times as many women as men have the disease.
- **Race/Ethnicity:** Rheumatoid arthritis occurs in all races and ethnic groups.

Symptoms

Common signs and symptoms of rheumatoid arthritis include:

- Tender, warm, swollen joints.
- Symmetrical pattern of affected joints.
- Joint inflammation often affecting the wrist and finger joints closest to the hand.
- Joint inflammation *sometimes* affecting other joints, including the neck, shoulders, elbows, hips, knees, ankles, and feet.
- Fatigue or low energy.
- Occasional fevers.
- Pain and stiffness lasting for more than 30 minutes in the morning or after a long rest.
- Symptoms that last for many years.

Rheumatoid arthritis affects people differently. Some people have mild or moderate forms of the disease. They have periods of worsening symptoms, called flares, and periods in which they feel better, called remissions. Others have a severe form of the disease that is active most of the time, lasts for many years or a lifetime, and leads to serious joint damage and disability.

Some people with rheumatoid arthritis also have other health problems:

- Many people develop anemia which is a decrease in the production of red blood cells.
- Less often, people have neck pain and dry eyes and mouth.
- Rarely, inflammation of the blood vessels, the lining of the lungs, or the sac enclosing the heart.
- Depression, anxiety, feelings of helplessness, and low self-esteem.

Causes

Scientists still do not know exactly what causes the immune system to turn against the body's own tissues in rheumatoid arthritis. Research over the last few years has begun to piece together the factors involved. These include:

***Genetic (inherited) factors*:**Scientists have discovered that certain genes known to play a role in the immune system are associated with rheumatoid arthritis. However, some people who have these particular genes never develop the disease. This suggests that genes are not the only factor in the development of rheumatoid arthritis. What is clear, however, is that more than one gene is involved in determining whether a person develops rheumatoid arthritis and how severe the disease will become.

***Environmental factors*:** Many scientists think that something must occur to trigger the disease

process in people whose genetic makeup puts them at risk for rheumatoid arthritis. Many factors have been suggested, but a specific one has not been confirmed.

***Other factors*:** Some scientists also think that hormonal factors, such as shortages or changes in certain sex hormones, may play a role when genetic and environmental factors also are involved. Scientists believe this because:

- Women are more likely to develop rheumatoid arthritis than men.
- The disease may improve during pregnancy and flare after pregnancy.
- Breastfeeding may worsen the disease.

We do not know all the answers, but we do know that rheumatoid arthritis develops from an interaction of many factors. Researchers are trying to understand these factors and how they work together.

Diagnosis

Rheumatoid arthritis can be difficult to diagnose in its early stages for several reasons:

- There is no single test for the disease.
- Symptoms differ from person to person and can be more severe in some people than in others.
- Symptoms can be similar to those of other types of arthritis and joint conditions, and it may take some time for other conditions to be ruled out.
- The disease develops over time, and only a few symptoms may be present in the early stages.

As a result, doctors use a variety of the following tools to diagnose the disease and to rule out other conditions.

Medical History

The doctor will begin by asking you to describe your symptoms, when and how they started, and how they have changed over time. The doctor will also ask about any other medical problems you and close family members have and about any medications you're taking. Answers to these questions can help the doctor make a diagnosis and understand the impact the disease has on your life.

Physical Examination

The doctor will:

- Check your reflexes and general health, including muscle strength.
- Examine bothersome joints and watch how you walk, bend, and carry out activities of daily

living.
- Look at your skin for a rash.
- Listen to your chest for signs of inflammation in the lungs.

Laboratory Tests

A number of lab tests may be useful in confirming a diagnosis of rheumatoid arthritis. Some of the common tests include:

- **Rheumatoid factor (RF):** This blood test checks for RF, an antibody most people with rheumatoid arthritis eventually have in their blood. (An antibody is a special protein made by the immune system that normally helps fight invaders in the body.) Not all people with rheumatoid arthritis test positive for RF, and some people test positive for RF but never develop the disease. RF also can be positive in some other diseases. However, a positive RF in a person who has symptoms consistent with rheumatoid arthritis can be useful in confirming a diagnosis. Also, high levels of RF are associated with more severe rheumatoid arthritis.
- **Anti-CCP antibodies:** This blood test detects antibodies to cyclic citrullinated peptide (anti-CCP). This test is positive in most people with rheumatoid arthritis and can even be positive years before rheumatoid arthritis symptoms develop. When used with the RF, this test's results are very useful in confirming a rheumatoid arthritis diagnosis.
- **Others:** Other common blood tests include:
    - White blood cell count.
    - Blood test for anemia, which is common in rheumatoid arthritis.
    - Erythrocyte sedimentation rate (often called the sed rate), which measures inflammation in the body.
    - C-reactive protein, another common test for inflammation that is useful both in making a diagnosis and monitoring disease activity and response to anti-inflammatory therapy.

Imaging Tests

Doctors use x-rays to see the degree of joint damage. They are not useful in the early stages of rheumatoid arthritis before damage is evident. Doctors may use them to rule out other causes of joint pain. X-rays may also be used later to monitor the progression of the disease. Magnetic resonance imaging (MRI) and ultrasound may be useful in identifying the early stages of rheumatoid arthritis and can help determine the severity of the disease.

Treatment

Doctors use a variety of approaches to treat rheumatoid arthritis. They may be used in combination and at different times during the course of the disease. Your doctor will choose treatments based on your situation.

No matter which treatment is chosen, the goals are the same:

- Relieve pain.
- Reduce inflammation.
- Slow down or stop joint damage.
- Improve well-being and ability to function.

To treat rheumatoid arthritis, doctors may suggest:

- Medications.
- Surgery.
- Routine monitoring and ongoing care.
- Complementary therapies.

Medications

Most people who have rheumatoid arthritis take medications. Studies show that early treatment with powerful drugs and drug combinations instead of one medication alone may be more effective in reducing or preventing joint damage than beginning with aspirin or other pain relievers. If you have persistent rheumatoid arthritis symptoms, see a doctor familiar with the disease and its treatment to reduce the risk of damage.

Many of the drugs used to treat rheumatoid arthritis reduce the inflammation that can cause pain and joint damage. However, inflammation is also one way the body fights infection and disease. But the level of risk is hard to judge because infections and cancer can occur in people with rheumatoid arthritis who are not on treatment. It is important to talk with your doctor about these risks.

Pain Relief and Anti-Inflammatory Drugs

Your doctor may prescribe some medications (analgesics) that only help with pain relief. Others, such as corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs), can reduce inflammation.

Disease-Modifying Anti-Rheumatic Drugs (DMARDS)

DMARDs may to slow the course of the disease. Common DMARDs your doctor may prescribe include:

- Hydroxychloroquine.
- Leflunomide.
- Methotrexate.
- Sulfasalazine.

Other DMARDs, called biologic response modifiers, may be used if your disease is more severe. These are genetically engineered medications that help reduce inflammation and damage to the joints by interrupting the inflammatory process. Currently, several biologic response modifiers are approved for rheumatoid arthritis, including:

- Abatacept.

- Adalimumab.
- Anakinra.
- Certolizumab.
- Etanercept.
- Golimumab.
- Infliximab.
- Rituximab.
- Tocilizumab.

Another DMARD, tofacitinib, is from a new class of drugs called jak kinase (JAK) inhibitors. It fights inflammation from inside the cell.

Surgery

The primary purpose of surgery is to reduce pain, improve the affected joint's function, and improve your ability to perform daily activities.

Surgery is not for everyone. Talk with your doctor and together decide what is the right choice for you. Discuss:

- Your overall health.
- The condition of the joint or tendon that will be operated on.
- The reason for, and the risks and benefits of the surgery.

Routine Monitoring and Ongoing Care

Regular medical care is important to monitor the course of the disease, determine the effectiveness and any negative effects of medications, and change therapies as needed.

Monitoring typically includes regular visits to the doctor. It also may include blood, urine, and other lab tests and x-rays.

Good communication between you and your doctor is necessary for effective treatment. Talking to the doctor regularly can help ensure that you receive:

- Necessary exercise and pain management programs.
- Necessary and appropriate medications.
- Information about surgical options if necessary.

Another factor to discuss with your doctor is the risk of osteoporosis, which is a condition in which bones become weakened and fragile. Having rheumatoid arthritis increases your risk of developing osteoporosis, particularly if you take corticosteroids. You may want to discuss with your doctor the potential benefits of calcium and vitamin D supplements or other osteoporosis treatments.

Complementary Therapies

Special diets, vitamins, and other complementary therapies are sometimes suggested to treat rheumatoid arthritis.

Research shows that some of these approaches, such as taking fish oil supplements, may help reduce inflammation. However, few, if any controlled scientific studies have been conducted on complementary approaches, and some studies have found no definite benefit to these therapies.

As with any therapy, you should discuss the benefits and risks with your doctor before beginning any complementary or new type of therapy. However, it is important not to neglect regular health care.

Who Treats

Diagnosing and treating rheumatoid arthritis requires a team effort involving you and several types of health care professionals. These may include:

- Internists, who specialize in the diagnosis and medical treatment of adults.
- Rheumatologists, who specialize in arthritis and other diseases of the bones, joints, and muscles.
- Orthopaedists, who specialize in the treatment of, and surgery for, bone and joint diseases or injuries.
- Physical therapists, who help to improve joint function.
- Occupational therapists, who teach ways to protect joints, minimize pain, perform activities of daily living, and conserve energy.
- Dietitians, who teach ways to eat a good diet to improve health and maintain a healthy weight.
- Nurse educators, who specialize in helping people understand their overall condition and implement their treatment plans.
- Mental health professionals, who help people cope with difficulties in the home and workplace that may result from their medical conditions.

Living With

Health care professionals can prescribe or recommend treatments to help you manage your rheumatoid arthritis However, research shows that people who take part in their own care report less pain and make fewer doctor visits. They also enjoy a better quality of life.

Self-management programs teach about rheumatoid arthritis and its treatments, exercise and relaxation approaches, communication between you and your health care team, and problem solving. Research on these programs has shown that they help people:

- Understand the disease.
- Reduce pain while remaining active.

- Cope physically, emotionally, and mentally.
- Have greater control over the disease and build a sense of confidence in the ability to function and lead full, active, and independent lives.

Lifestyle Changes

Certain activities can help improve your ability to function on your own and maintain a positive outlook.

- Rest and exercise: Balance your rest and exercise, with more rest when the disease is active and more exercise when it is not. Rest helps to reduce active joint inflammation and pain and to fight fatigue. In general, shorter rest breaks every now and then are more helpful than long times spent in bed. Exercise is important for maintaining healthy and strong muscles, preserving joint mobility, and maintaining flexibility. Exercise can also help you sleep well, reduce pain, maintain a positive attitude, and manage weight. An exercise program should take into account your physical abilities, limitations, and changing needs.
- Joint care: Some people find wearing a splint for a short time around a painful joint reduces pain and swelling. People use splints mostly on wrists and hands, but also on ankles and feet. A doctor or a physical or occupational therapist can help you choose a splint and make sure it fits properly. Other ways to reduce stress on joints include:
    - Self-help devices (for example, zipper pullers or long-handled shoe horns).
    - Devices to help with getting on and off chairs, toilet seats, and beds.
    - Changes in the ways you carry out daily activities.
- Stress reduction: The emotions you may feel because of the disease, fear, anger, and frustration, combined with any pain and physical limitations can increase your stress level. Although there is no evidence that stress plays a role in causing rheumatoid arthritis, it can make living with the disease more difficult. Stress also may affect the amount of pain you feel. Ways to cope with stress include:
    - Regular rest periods.
    - Relaxation, distraction, or visualization exercises.
    - Exercise programs.
    - Participation in support groups.
    - Good communication with your health care team.
- Healthful diet: With the exception of several types of oils, there is no scientific evidence that any specific food or nutrient helps or harms people with rheumatoid arthritis. However, an overall nutritious diet with balanced calories, protein, and calcium is important. You may need to be careful about drinking alcoholic beverages because they may interact with the medications you take for rheumatoid arthritis. If you take methotrexate you may need to avoid alcohol altogether, because one of the most serious possible long-term side effects of methotrexate is liver damage. Alcohol use can make it worse.
- Climate: Some people notice that their rheumatoid arthritis gets worse when there is a sudden change in the weather. However, there is no evidence that a specific climate can prevent or reduce the effects of rheumatoid arthritis. Moving to a new place with a different climate usually does not make a long-term difference in a person’s rheumatoid arthritis.

Research Progress

Over the last several decades, research has greatly increased our understanding of the immune system, genetics, and biology. This research is now showing results in several areas important to rheumatoid arthritis. Scientists are thinking about rheumatoid arthritis in exciting ways that were not possible years ago.

Genetics

NIAMS-supported researchers have identified several genetic factors that predispose some people to develop rheumatoid arthritis, as well as factors connected to disease severity. Scientists know that more than one gene is involved in determining whether a person develops rheumatoid arthritis and how severe the disease will become.

An international research team identified dozens of new areas in the human genome associated with rheumatoid arthritis and found that many are already the targets of drugs approved for other conditions. The findings hint at new treatment approaches for the disease.

Researchers are investigating the potential connection between health, disease, and the human microbiome, which is the entire population of microorganisms that inhabit the human body. One study found that the presence of a specific type of gut bacteria correlated with rheumatoid arthritis in newly diagnosed, untreated people. The finding suggests a potential role for the bacteria in the disease.

The Disease Process

NIAMS intramural researchers are studying the natural history of rheumatoid arthritis in children and adults in an effort to understand how the disease progresses and impacts patient symptoms and functional status.

Investigators are also exploring whether patients with rheumatoid arthritis in remission while taking tumor necrosis factor-alpha (TNF-?) inhibitors can remain in remission after withdrawal of these medications. In addition, investigators are attempting to identify predictors of relapse in these individuals.

Scientists are continuing to understand the molecular underpinnings of rheumatoid arthritis and are working to develop tests that could help diagnose rheumatoid arthritis earlier and identify patients who would benefit most from specific treatments.

New Therapies

Researchers continue to identify molecules that appear to play a role in rheumatoid arthritis and thus are potential targets for new treatments. The path between identifying the molecule and developing a drug that targets it is long and difficult. Fortunately, this path has been successfully negotiated, and new drugs have emerged that successfully reduce symptoms and damage in

rheumatoid arthritis. Researchers continue to identify more candidate drugs, with hopes that these will have fewer side effects or will cure more patients.

- ***Tofacitinib:*** Tofacitinib, approved for the treatment of rheumatoid arthritis in 2012, was from a new class of drugs developed to target Janus kinases. One member of this family, JAK3, was discovered in the early 1990s by a National Institutes of Health (NIH) laboratory at the NIAMS. Subsequent studies carried out at the National Heart, Lung, and Blood Institute (NHLBI), in collaboration with the NIAMS, showed that genetic defects in JAK3 can cause severe combined immunodeficiency. This discovery led to the idea that drugs blocking Janus kinases would suppress the immune system and might be protective against the damaging inflammation of rheumatoid arthritis and certain other autoimmune diseases.
- ***NIH AMP Program:*** The NIAMS is leading the Accelerating Medicines Partnership in Rheumatoid Arthritis and Lupus (AMP RA/Lupus). The goal of this program is to integrate data from multiple genome-wide analytic approaches to generate a comprehensive understanding of the mechanisms of tissue damage in rheumatoid arthritis and lupus.
- ***Joint inflammation:***NIAMS-funded researchers have determined that joint inflammation can continue in rheumatoid arthritis, even after clinical symptoms have eased. This finding may help doctors determine when a patient is truly in remission and can safely stop treatment.

Related Resources

U.S. Food and Drug Administration
Toll free: 888-INFO-FDA (888-463-6332)
Website: https://www.fda.gov

Drugs@FDA at https://www.accessdata.fda.gov/scripts/cder/daf/. Drugs@FDA is a searchable catalog of FDA-approved drug products.

Centers for Disease Control and Prevention, National Center for Health Statistics
Website: https://www.cdc.gov/nchs

National Institute of Allergy and Infectious Diseases
Website:https://www.niaid.nih.gov/Pages/default.aspx

National Center for Complementary and Integrative Health
Website: https://nccih.nih.gov

American Academy of Orthopaedic Surgeons
Website: https://www.aaos.org

American College of Rheumatology
Website: https://www.rheumatology.org

Arthritis Foundation

Website: https://www.arthritis.org

If you need more information about available resources in your language or other languages, please visit our webpages below or contact the NIAMS Information Clearinghouse at NIAMSInfo@mail.nih.gov.

- Asian Language Health Information
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